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EXAMINER	
LANDSMAN, ROBERT S	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,917	CADET ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *3,5,11,13 and 15-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-10,12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/9/03; 7/12/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison*.

DETAILED ACTION

1. Formal Matters

A. The Election dated 7/14/04 has been entered into the record.

B. Claims 1-32 are pending in the application and were subject to restriction in the Office Action mailed 6/14/04. In the Response dated 7/14/04, Applicants elected Group I, claims 1-14 without traverse and limited the invention to elected SEQ ID NO:1. Therefore, claims encompassing SEQ ID NO:1, which are claims 1, 2, 4, 6-10, 12 and 14, are the subject of this Office Action.

C. The Information Disclosure Statements dated 7/12/02 and 6/9/03 have been entered into the record.

2. Specification

A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Nucleic acids encoding opiate receptors.

B. According to 37 CFR 1.821(d) (MPEP § 2422), where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Sequences appear on page 2, line 22 of the specification but are not identified by SEQ ID NO as required.

C. The specification is objected to due to the use of hyperlinks, for example, on page 9, lines 13-15. Applicant is advised that embedded hyperlinks and/or other forms of browser-executable code are impermissible and require deletion. The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01(p), paragraph I regarding incorporation by reference.

3. Claim Objections

A. Claims 4 and 12 are objected to since they recite non-elected SEQ ID NO:3 in the claims.

4. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 1, 2, 4, 6-10, 12 and 14 are rejected under 35 USC 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. These claims are directed to SEQ ID NO:1. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published 1/5/01, 66 FR 1092. The instant application has provided a description of an isolated protein. However, the instant application does not disclose a specific and substantial biological role of this protein or its significance.

Applicants have not disclosed a full-length mu3 opioid receptor polypeptide, or encoding polynucleotide. SEQ ID NO:1 is only 81 bases in length. Applicants have not demonstrated that this nucleic acid molecule encodes a protein with mu3 opioid receptor function. Furthermore, since the nucleic acid molecule has no utility, the cell comprising this nucleic acid molecule also has no utility.

5. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 1, 2, 4, 6-10, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

B. Claims 1, 2, 4, 6-10, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding the mu opioid receptors of SEQ ID NO:5, 7, 9 and 11, does not reasonably provide enablement for polynucleotides encoding all mu3 opioid receptors, including those which do not hybridize to SEQ ID NO:12 and 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all polynucleotides encoding all "**mu3 opioid receptors**," including those which "**do not hybridize**" to SEQ ID NO:12 and 13. These nucleic acid molecules would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the polynucleotide of SEQ ID NO:4, 6, 8 and 10 and would encode proteins which have one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:5, 7, 9 and 11.

Applicants provide only minimal guidance and working examples of nucleic acid molecules which encode mu3 opioid receptors. In addition, **SEQ ID NO:1 is only 81 nucleotides**, which does not encode a full-length receptor. **It is also not clear if SEQ ID NO:1 does or does not hybridize to SEQ ID NO:12 and 13**. Furthermore, none of the claims provides a *function* of these nucleic acid molecules other than the fact that they must have an "**activity**." Applicants have provided no guidance as to what critical residues are required to maintain the functional characteristics of a mu3 opioid receptor, including the fragment of SEQ ID NO:1. Therefore, polynucleotides which meet the limitations of, for example, claim 2, would only be fragments of a full-length receptor. Furthermore, it is not predictable to one of ordinary skill in the art how to make a functional mu3 opioid receptor which is less than the full-length of a mu3 opioid receptor (i.e. SEQ ID NO:1).

Furthermore, the claims recite "a cell comprising the isolated nucleic acid molecule..." The claims are rejected since they read on **gene therapy**. Applicants are required to amend the claims to recite "an isolated cell comprising..."

In summary, the breadth of the claims is excessive with regard to Applicants claiming all nucleic acids which encode mu3 opioid receptors. There is also only minimal guidance and working examples of

these nucleic acid molecules and proteins and no guidance as to which residues are critical for protein function. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make a functional opioid receptor other than those encoded by SEQ ID NO:4, 6, 8 and 10, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1, 2, 4, 6-10, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Nucleic acid molecules encompassed by the claims would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the polynucleotide of SEQ ID NO:1. These nucleic acid molecules would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:1. In addition, **SEQ ID NO:1 is only 81 nucleotides**, which does not encode a full-length receptor. **It is also not clear if SEQ ID NO:1 does or does not hybridize to SEQ ID NO:12 and 13**. If not, none of these species has been described. Furthermore, claim 1 encompasses the genus of all mu3 opioid receptors, including those from any species.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "mu3 opioid receptor," "SEQ ID NO:1," or molecules which "do not hybridize to SEQ ID NO:12 and 13" (which could be at least thousands of molecules) alone are insufficient to describe the genus. The specification provides a written description of only a partial mu3 opioid receptor polynucleotide (SEQ ID NO:1). No other species are described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical nucleic acid residues which

would structurally characterize the genus of nucleic acids encoding the genus of mu3 opioid receptors claimed, because it is unknown and not described what structurally constitutes any different nucleic acids encoding mu3 receptors, or nucleic acids encoding mu3 receptors from any different species, which are further not described,; thereby not meeting the written description requirement under 35 USC 112, first paragraph. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

7. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 1, 2, 4, 6-10, 12 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The metes and bounds of "activity" are not known. Binding a ligand, for example, is an activity. However, this activity would not clearly define the function, or identify, of a mu3 opioid receptor.

B. Claim 4, 6, 12 and 14 are vague and indefinite since the claim recites "hybridizes." It is not known what these hybridization conditions are. Nucleic acid molecules which hybridize under conditions of "low" stringency would not necessarily hybridize under conditions of "high" stringency. Furthermore, not all conditions of "high" or "low" stringency, for example, are the same. Therefore, it is required that Applicants amend the claims to recite the exact hybridization conditions without using indefinite phrases such as "*for example*" **without adding new matter.**

8. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

A. Claims 6 and 7 are rejected under 35 U.S.C. 102(a) as being anticipated by Birren (Accession No. AC027439). The claims recite a nucleic acid molecule which hybridizes to a nucleic acid molecules encoding a mu3 opioid receptor, or which is identical to SEQ ID NO:1. Birren teach a nucleic acid molecule which is 100% identical to SEQ ID NO:1. In absence of evidence to the contrary, this sequence does not hybridize to SEQ ID NO:12 or 13.

9. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Birren et al. in view of Sibson et al. (WO 95/01548). The claim recites a polynucleotide in a cell. The teachings of Birren et al. are seen in the above rejection under 35 USC 102. Birren et al. do not teach cells. However, Sibson et al. do teach cells (page 7, line 39 – page 9, line 10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Sibson et al. by substituting a cDNA in the polycloning region of the vector with the polynucleotide (cDNA) of Birren et al. for the purpose of transfecting a host cell as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so (pages 8-13). One of ordinary skill in the art would have been motivated to make this substitution in order to express the protein encoded by the introduced DNA in a host cell to perform ligand binding and functional assays. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make this invention since these techniques are widely used in the art and are highly successful (Sibson et al., page 10, line 38 – page 12, line 42). The present invention, therefore, is *prima facia* obvious over the above references in the absence of evidence to the contrary.

10. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (571) 272-0888. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Fax draft or informal communications with the examiner should be directed to (571) 273-0888.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-0700.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
August 23, 2004

ROBERT LANDSMAN
PATENT EXAMINER